09/135 425
AH 6-4-1

1. Document ID: US 6037450 A

L1: Entry 1 of 16 File: USPT Mar 14, 2000

US-PAT-NO: 6037450
DOCUMENT-IDENTIFIER: US 6037450 A
TITLE: Diagnostic assays using soluble endothelial cell protein C/activated protein C receptor
DATE-ISSUED: March 14, 2000

US-CL-CURRENT: 530/350; 530/827, 530/830

APPL-NO: 9/ 082021
DATE FILED: May 20, 1998

PARENT-CASE:
This application is a divisional of U.S. Ser. No. 08/884,203, filed Jun. 27, 1997.

IN: Esmon; Charles T., Stearns-Kurosawa; Deborah J., Kurosawa; Shinichiro

AB: Plasma EPCR has been isolated, characterized and shown to block cellular protein C activation and
APC anticoagulant activity. Plasma EPCR appears to be about 43,000 daltons and circulates at approximately
100 ng/ml (98.4.+-.27.8 ng/ml, n=22). Plasma EPCR bound activated protein C with an affinity similar to that
of recombinant soluble EPCR (Kd.sub.app approximately 30 nM), and inhibits both protein C activation on an
endothelial cell line and APC anticoagulant activity in a one-stage factor Xa clotting assay. Soluble plasma
EPCR appears to attenuate the membrane-bound EPCR augmentation of protein C activation and the anticoagulant
function of activated protein C. Soluble EPCR has also been detected in urine. Levels of soluble EPCR can
rise in inflammatory disease associated with vascular injury and appear to be correlated with inflammation
and disease states associated with abnormal coagulation. Since EPCR expression is restricted to larger
vessels and is usually negative in cappillaries, these observations provide a mechanism for analyzing
injury/stimulation of large vessel endothelial cells.

2. Document ID: US 5852171 A

L1: Entry 2 of 16 File: USPT Dec 22, 1998

US-PAT-NO: 5852171
DOCUMENT-IDENTIFIER: US 5852171 A
TITLE: Cloning and regulation of an endothelial cell protein C/activated protein C receptor
DATE-ISSUED: December 22, 1998

US-CL-CURRENT: 530/350; 530/380

APPL-NO: 8/ 878283
DATE FILED: June 18, 1997

PARENT-CASE:
This is a divisional of U.S. Ser. No. 08/289,699, filed on Aug. 12, 1994, now U.S. Pat. No. 5,695,993.

IN: Fukudome; Kenji, Esmon; Charles T.

AB: Human protein C and activated protein C were shown to bind to endothelium specifically,
selectively and saturably (Kd=30 nM, 7000 sites per cell) in a Ca.sup.2+ dependent fashion. Expression
cloning revealed a 1.3 kb CDNA that coded for a novel type I transmembrane glycoprotein capable of binding
protein C. This protein appears to be a member of the CD1/MHC superfamily. Like thrombomodulin, the receptor
involved in protein C activation, the endothelial cell protein C receptor (EPCR) function and message are
both down regulated by exposure of endothelium to TNF. Identification of EPCR as a member of the CD1/MHC
superfamily provides insights into the role of protein C in regulating the inflammatory response, and
determination of methods for pharmaceutical use in manipulating the inflammatory response.

3. Document ID: US 5804392 A

L1: Entry 3 of 16 File: USPT Sep 8, 1998

US-PAT-NO: 5804392
DOCUMENT-IDENTIFIER: US 5804392 A
TITLE: Diagnostic assays using soluble endothelial cell protein C/activated protein C receptor
DATE-ISSUED: September 8, 1998

US-CL-CURRENT: 435/7.1; 435/7.8, 435/975, 436/506, 530/387.1, 530/388.22, 530/389.1

APPL-NO: 8/ 884203
DATE FILED: June 27, 1997

IN: Esmon; Charles T., Stearns-Kurosawa; Deborah J., Kurosawa; Shinichiro

AB: Plasma EPCR has been isolated, characterized and shown to block cellular protein C activation and
APC anticoagulant activity. Plasma EPCR appears to be about 43,000 daltons and circulates at approximately
100 ng/ml (98.4.+-.27.8 ng/ml, n=22). Plasma EPCR bound activated protein C with an affinity similar to that
of recombinant soluble EPCR (Kd.sub.app approximately 30 nM), and inhibits both protein C activation on an
endothelial cell line and APC anticoagulant activity in a one-stage factor Xa clotting assay. Soluble plasma
EPCR appears to attenuate the membrane-bound EPCR augmentation of protein C activation and the anticoagulant
function of activated protein C. Soluble EPCR has also been detected in urine. Levels of soluble EPCR can
rise in inflammatory disease associated with vascular injury and appear to be correlated with inflammation
and disease states associated with abnormal coagulation. Since EPCR expression is restricted to larger
vessels and is usually negative in cappillaries, these observations provide a mechanism for analyzing
injury/stimulation of large vessel endothelial cells.

4. Document ID: US 5695993 A

L1: Entry 4 of 16 File: USPT Dec 9, 1997

US-PAT-NO: 5695993
DOCUMENT-IDENTIFIER: US 5695993 A
TITLE: Cloning and regulation of an endothelial cell protein C/activated protein C receptor
DATE-ISSUED: December 9, 1997

US-CL-CURRENT: 435/325; 435/320.1, 435/69.1, 536/23.5

APPL-NO: 8/ 289699
DATE FILED: August 12, 1994

IN: Fukudome; Kenji, Esmon; Charles T.

AB: Human protein C and activated protein C were shown to bind to endothelium specifically,
selectively and saturably (Kd=30 nM, 7000 sites per cell) in a Ca.sup.2+ dependent fashion. Expression
cloning revealed a 1.3 kb CDNA that coded for a novel type I transmembrane glycoprotein capable of binding
protein C. This protein appears to be a member of the CD1/MHC superfamily. Like thrombomodulin, the receptor
involved in protein C activation, the endothelial cell protein C receptor (EPCR) function and message are
both down regulated by exposure of endothelium to TNF. Identification of EPCR as a member of the CD1/MHC
superfamily provides insights into the role of protein C in regulating the inflammatory response, and
determination of methods for pharmaceutical use in manipulating the inflammatory response.

5. Document ID: US 5548796 A

L1: Entry 5 of 16 File: USPT Aug 20, 1996

US-PAT-NO: 5548796
DOCUMENT-IDENTIFIER: US 5548796 A
TITLE: Method of automatic retransmission of frames in a local area network
DATE-ISSUED: August 20, 1996

US-CL-CURRENT: 710/52; 370/447

APPL-NO: 8/ 237822
DATE FILED: May 4, 1994

PARENT-CASE:
This is a divisional of application Ser. No. 08/147,348, filed Nov. 2, 1993, now abandoned.

IN: Ketchum; Kevin D.

AB: A configurable network interface controller that provides for the automatic retransmission of
collided Ethernet frames from a local RAM while observing two modes of operation: (1) retransmission of as
much of the frame as possible without violating latency requirements and
(2) first guaranteeing the safe
retransmission of the first 64 bytes and then returning to observation of the latency requirements.

6. Document ID: US 5513376 A

L1: Entry 6 of 16 File: USPT Apr 30, 1996

US-PAT-NO: 5513376
DOCUMENT-IDENTIFIER: US 5513376 A
TITLE: Method of operating an extension FIFO in another device when it is full by periodically re-initiating a
write operation until data can be transferred
DATE-ISSUED: April 30, 1996

US-CL-CURRENT: 710/53; 364/238.7, 364/239.1, 364/239.6, 364/DIG.1, 365/220, 365/221, 710/2, 710/34, 710/52

APPL-NO: 8/ 238260
DATE FILED: May 4, 1994

PARENT-CASE:
This is a division application of application Ser. No. 08/147,348 filed on Nov. 2, 1993 now abandoned.

IN: Lohmeyer; Michael G.

AB: A configurable network interface controller provides a multi-chip FIFO extension protocol.
Utilizing this protocol, FIFOs that are physically separated (e.g., in separate chips) can be made to operate
as though they are a single FIFO.

7. Document ID: US 5495593 A

L1: Entry 7 of 16 File: USPT Feb 27, 1996

US-PAT-NO: 5495593
DOCUMENT-IDENTIFIER: US 5495593 A
TITLE: Microcontroller device having remotely programmable EPROM and method for programming
DATE-ISSUED: February 27, 1996

US-CL-CURRENT: 711/103; 364/DIG.1, 711/147

APPL-NO: 8/ 254656
DATE FILED: June 3, 1994

PARENT-CASE:
This is a continuation of application Ser. No. 08/056,737 filed Apr. 28, 1993 which was an FWC of application Ser.
No. 07/545,910 filed on Jun. 29, 1990 which is now abandoned.

IN: Elmer; Thomas I., Nguyen; Tuan T., Lin; Rung-Pan

AB: A microcontroller device on a single integrated circuit including a central processing unit, an
associated data bus and an electrically-programmable nonvolatile memory is disclosed. The nonvolatile memory
contains the applications program and may be remotely programmed by way of a communication port, such as a
universal asynchronous, receiver/transmitter (UART) device, utilizing a separate host computer. A second
nonvolatile memory is provided which contains a control program which is executed by the central processing
unit for carrying out the programming of the electrically-programmable nonvolatile memory utilizing data and
address information received from the host computer over the communications port.

8. Document ID: US 4566124 A

L1: Entry 8 of 16 File: USPT Jan 21, 1986

US-PAT-NO: 4566124
DOCUMENT-IDENTIFIER: US 4566124 A
TITLE: Pattern reading system
DATE-ISSUED: January 21, 1986

US-CL-CURRENT: 382/185; 382/197, 382/316

APPL-NO: 6/ 521956
DATE FILED: August 10, 1983

FOREIGN-APPL-PRIORITY-DATA:
COUNTRY APPL-NO APPL-DATE
JP 57-139059 August 10, 1982

IN: Yamamoto; Kazuhiko, Saito; Taiichi

AB: A pattern reading system by line segment approximation comprising the steps of tracing the contour
and simultaneously, seeking out as candidate extreme points the points at which the inner products of
coordinate point vectors and directional vectors at coordinate points of the contour being traced are
largest, and feeding out these candidate extreme points as real extreme points when the differences between
the inner products of the direction vectors and the inner products of the candidate extreme points are
greater than an allowance set in advance.

9. Document ID: US 5804392 A

L1: Entry 9 of 16 File: EPAB Sep 8, 1998

PUB-NO: US005804392A
DOCUMENT-IDENTIFIER: US 5804392 A
TITLE: Diagnostic assays using soluble endothelial cell protein C/activated protein C receptor

PUBN-DATE: September 8, 1998

INT-CL (IPC): G01N 33/53; G01N 33/564; C07K 16/28

APPL-NO: US88420397
APPL-DATE: June 27, 1997
PRIORITY-DATA: US88420397A (June 27, 1997)

IN: ESMON, CHARLES T, STEARNS-KUROSAWA, DEBORAH J, KUROSAWA, SHINICHIRO

AB: Plasma EPCR has been isolated, characterized and shown to block cellular protein C activation and
APC anticoagulant activity. Plasma EPCR appears to be about 43,000 daltons and circulates at approximately
100 ng/ml (98.4+/-27.8 ng/ml, n=22). Plasma EPCR bound activated protein C with an affinity similar to that
of recombinant soluble EPCR (Kdapp approximately 30 nM), and inhibits both protein C activation on an
endothelial cell line and APC anticoagulant activity in a one-stage factor Xa clotting assay. Soluble plasma
EPCR appears to attenuate the membrane-bound EPCR augmentation of protein C activation and the anticoagulant
function of activated protein C. Soluble EPCR has also been detected in urine. Levels of soluble EPCR can
rise in inflammatory disease associated with vascular injury and appear to be correlated with inflammation
and disease states associated with abnormal coagulation. Since EPCR expression is restricted to larger
vessels and is usually negative in cappillaries, these observations provide a mechanism for analyzing
injury/stimulation of large vessel endothelial cells.

10. Document ID: WO 9820041 A1

L1: Entry 10 of 16 File: EPAB May 14, 1998

PUB-NO: WO009820041A1
DOCUMENT-IDENTIFIER: WO 9820041 A1
TITLE: ENDOTHELIUM SPECIFIC EXPRESSION REGULATED BY EPCR CONTROL ELEMENTS

PUBN-DATE: May 14, 1998

INT-CL (IPC): C07K 14/705
EUR-CL (EPC): C07K014/705

APPL-NO: US09720364
APPL-DATE: November 7, 1997
PRIORITY-DATA: US03071896P (November 8, 1996)

IN: ESMON, CHARLES T, GU, JIAN-MING

AB: The promoter of the EPCR gene has been isolated from both murine (SEQ. ID No. 1) and human (SEQ.
ID No. 2) genomic libraries. The promoter has been demonstrated to include a region which results in
selective expression in endothelial cells, between -1 and -220 based on

the positions relative to the ATG
encoding the first amino acid of the murine EPCR protein (nucleotides 3130 to 3350 of SEQ. ID No. 1), and a
region which selectively results in expresion in large vessel endothelial cells, as opposed to all
endothelial cells, located between -700 and -1080 (nucleotides 2270 to 2840 of SEQ. ID No. 1). A thrombin
responsive element has been identified in the EPCR promoter, from -337 to -345 in the murine promoter
(nucleotides 3007 to 3014 SEQ. ID No. 1) and from -360 to -368 (nucleotides 2722 to 2729 SEQ. ID No. 2) in
the human promoter. The sequence is CCCACCCC (SEQ. ID No. 3). A serum response element has also been
identified between -280 and -350 (nucleotides 2990 to 3061 of SEQ. ID No. 1). The regulatory sequences
present in the EPCR promoter can be used in combination with genes encoding other proteins, as well as
shorter oligonucleotides, to increase expression by exposure to thrombin or serum or to effect selective
expression in endothelial cells generally or preferentially in endothelial cells of the large blood vessels.
The gene control elements include elements responsive to environmental stiumuli (either thrombin or serum);
and information to determine distribution of the desired protein expression (large vessels). Therapeutic
strategies include the use of the minimal promoter (-220 to -1) for expression in all endothelial cells, for
example, for any kind of gene therapy where systemic distribution is desired; the use of a promoter including
an environmental stimuli response element(s), for use in delivery of agents whose expression should be
increased during times of increased thrombin/platelet activation or during regional trauma; the use of the
minimal promoter including an environmental stimuli response element and the element directing expression to
large vessel endothelium, where a response to regional trauma is desirable but only in large vessel
endothelium, and the use of the minimal promoter and element directing expression to large vessel
endothelium, where expresion is specifically targeted to large vessel endothelium but is not increased in
response to any particular stimuli.

11. Document ID: US 5695993 A

L1: Entry 11 of 16 File: EPAB Dec 9, 1997

PUB-NO: US005695993A
DOCUMENT-IDENTIFIER: US 5695993 A
TITLE: Cloning and regulation of an endothelial cell protein C/activated protein C receptor

PUBN-DATE: December 9, 1997

INT-CL (IPC): C12N 5/16; C07H 21/04
EUR-CL (EPC): C07K014/705

APPL-NO: US28969994
APPL-DATE: August 12, 1994
PRIORITY-DATA: US28969994A (August 12, 1994)

IN: FUKUDOME, KENJI, ESMON, CHARLES T

AB: Human protein C and activated protein C were shown to bind to endothelium specifically,
selectively and saturably (Kd=30 nM, 7000 sites per cell) in a Ca2+ dependent fashion. Expression cloning
revealed a 1.3 kb CDNA that coded for a novel type I transmembrane glycoprotein capable of binding protein C.
This protein appears to be a member of the CD1/MHC superfamily. Like thrombomodulin, the receptor involved in
protein C activation, the endothelial cell protein C receptor (EPCR) function and message are both down
regulated by exposure of endothelium to TNF. Identification of EPCR as a member of the CD1/MHC superfamily
provides insights into the role of protein C in regulating the inflammatory response, and determination of
methods for pharmaceutical use in manipulating the inflammatory response.

12. Document ID: WO 9605303 A1

L1: Entry 12 of 16 File: EPAB Feb 22, 1996

PUB-NO: WO009605303A1
DOCUMENT-IDENTIFIER: WO 9605303 A1
TITLE: CLONING AND REGULATION OF AN ENDOTHELIAL CELL PROTEIN C/ACTIVATED PROTEIN C RECEPTOR

PUBN-DATE: February 22, 1996

INT-CL (IPC): C12N 15/12; C07K 14/705; A61K 39/395; C12N 15/11; A61K 38/17; C07K 16/28; G01N 33/68
EUR-CL (EPC): C07K014/705

APPL-NO: US09509636
APPL-DATE: August 9, 1995
PRIORITY-DATA: US28969994A (August 12, 1994)

IN: FUKUDOME, KENJI, ESMON, CHARLES T

AB: Human protein C and activated protein C were shown to bind to endothelium specifically,
selectively and saturably (Kd=30 nM, 7000 sites per cell) in a Ca<2+> dependent fashion. Expression cloning
revealed a 1.3 kb CDNA that coded for a novel type I transmembrane glycoprotein capable of binding protein C.
This protein appears to be a member of the CD1/MHC superfamily. Like thrombomodulin, the receptor involved in
protein C activation, the endothelial cell protein C receptor (EPCR) function and message are both down
regulated by exposure of endothelium to TNF. Identification of EPCR as a member of the CD1/MHC superfamily
provides insights into.the role of protein C in regulating the inflammatory response, and determination of
methods for pharmaceutical use in manipulating the inflammatory response.

13. Document ID: DE 19751465 C2, DE 19751465 A1, WO 9927706 A1

L1: Entry 13 of 16 File: DWPI Sep 2,

1999

DERWENT-ACC-NO: 1999-328210
DERWENT-WEEK: 199939

TITLE: Sensitivity values determination unit for copying images taken by digital camera

PRIORITY-DATA:
1997DE-1051465
November 20, 1997

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
DE 19751465 C2	September 2, 1999	N/A	000	H04N001/40
DE 19751465 A1	May 27, 1999	N/A	005	H04N001/40
WO 9927706 A1	June 3, 1999	G	000	H04N001/60

APPLICATION-DATA:

PUB-NO	APPL-DATE	APPL-NO	APPL-DESCRIPTOR
DE19751465C2	November 20, 1997	1997DE-1051465	N/A
DE19751465A1	November 20, 1997	1997DE-1051465	N/A
WO 9927706A1	November 17, 1998	1998WO-EP07385	N/A

INT-CL (IPC): H04N 1/32; H04N 1/40; H04N 1/60

IN: FINDEIS, G, FUERSICH, M, KEUPP, W

AB: NOVELTY - The unit comprises a recognition module (EP,CR) of the type of digital camera (KT1...N)
which has taken the image. A control (CR) determines the sensitivity values in dependence on the recognized
type. There is a memory (SP2) for several copying data sets (GD1...N), containing sensitivity values for
image copying from different camera types., DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a
determinatio n method., USE - For fotoprinter, minilab or computer controlled printer., ADVANTAGE - Precise
and naturally true reproduction of images taken by digital camera., DESCRIPTION OF DRAWING(S) - The figure
presents example of the unit., recognition module EP,CR, camera type KT, control CR, copying data sets. GD

14. Document ID: AU 9882694 A, US 5804392 A, WO 9900673 A1
L1: Entry 14 of 16
File: DWPI
Jan 19, 1999

DERWENT-ACC-NO: 1998-505645
DERWENT-WEEK: 199922

TITLE: Immuno-based detection of protein C receptor - useful in the diagnosis of inflammatory and coagulation
states and disorders associated with damage to endothelium and large blood vessel disease

PRIORITY-DATA:
1997US-0884203
June 27, 1997

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
AU 9882694 A	January 19, 1999	N/A	000	G01N033/68
US 5804392 A	September 8, 1998	N/A	023	G01N033/53
WO 9900673 A1	January 7, 1999	E	000	G01N033/68

APPLICATION-DATA:

PUB-NO	APPL-DATE	APPL-NO	APPL-DESCRIPTOR
AU 9882694A	June 26, 1998	1998AU-0082694	N/A
AU 9882694A	N/A	WO 9900673	Based on
US 5804392A	June 27, 1997	1997US-0884203	N/A
WO 9900673A1	June 26, 1998	1998WO-US13385	N/A

INT-CL (IPC): C07K 14/705; C07K 16/28; G01N 33/53; G01N 33/564; G01N 33/68

IN: ESMON, C T, KUROSAWA, S, STEARNS-KUROSAWA, D J

AB: An assay for soluble endothelial protein C receptor comprises containing a sample from a patient to be tested and measuring the amount of soluble endothelial protein C receptor., Also claimed is a kit for detection and measurement of endothelial protein C receptor comprising:, (a) an antibody immunoreactive with endothelial protein C receptor;, (b) reagents to detect a reaction between the Ab and endothelial protein C receptor in a patient sample; and, (c) standards to correlate the amount of reaction to normal and abnormal levels of endothelial protein C receptor., USE - The assay is used for the diagnosis of coagulation and inflammatory states and disorders, damage to endothelium, and large blood vessel disease, e.g. autoimmune diseases, transplantation, sepsis, shock, pre-eclampsia, diabetes, vascular disease (especially cardiopulmonary bypass, unstable angina, restenosis and angioplasty), kidney disease and liver disease (claimed). Protein C is involved in the regulation of a host response to inflammation. The protein is one of the last components to be activated in the coagulation system, and is thought to control coagulation and inflammation. Activation of the receptor through a pathway involving thrombin, activates protein C. The protein C pathway is apparently only involved in large blood vessels, not capillaries, and so is activated with for major vascular conditions, and the increased presence of the receptor in the conditions stated makes it ideal as a diagnostic component.

15. Document ID: EP 937104 A1, WO 9820041 A1, AU 9854317 A

L1: Entry 15 of 16 File: DWPI Aug 25, 1999

DERWENT-ACC-NO: 1998-286871
DERWENT-WEEK: 199939

TITLE: Regulatory elements from the endothelial protein C receptor promoter - useful to direct expression of genes or nucleotide molecules e.g. to endothelial cells or only large vessel endothelial cells in gene therapy

PRIORITY-DATA:

1997US-0054533	August 4, 1997
1996US-0030718	November 8, 1996

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
EP 937104 A1	August 25, 1999	E	000	C07K014/705
WO 9820041 A1	May 14, 1998	E	069	C07K014/705
AU 9854317 A	May 29, 1998	N/A	000	C07K014/705

APPLICATION-DATA:

PUB-NO	APPL-DATE	APPL-NO	APPL-DESCRIPTOR
EP 937104A1	November 7, 1997	1997EP-0948205	N/A
EP 937104A1	November 7, 1997	1997WO-US20364	N/A
EP 937104A1	N/A	WO 9820041	Based on
WO 9820041A1	November 7, 1997	1997WO-US20364	N/A
AU 9854317A	November 7, 1997	1998AU-0054317	N/A
AU 9854317A	N/A	WO 9820041	Based on

INT-CL (IPC): C07K 14/705

IN: ESMON, C T, GU, J

AB: Regulatory elements (I) isolated from the endothelial protein C receptor (EPCR) promoter which directs expression selectively to endothelial cells are new. Also claimed are constructs for heterologous gene expression comprising (I), USE - The regulatory elements are useful to control expression of a gene/biologically active nucleotide molecule (claimed), by expressing these under control of one of the elements (optionally with the thrombin response element) (claimed). Expression of the gene/nucleotide molecule is selectively in large vessel endothelial cells and/or as a result of environmental stimuli (either thrombin or serum) can be achieved by inclusion of the appropriate regulatory element(s). Atherosclerosis and most other vascular diseases primarily occur in large vessels, and for gene therapy for such diseases it is desirable to target endothelial cells, the primary defence mechanism against cellular infiltration and thrombosis. The constructs are therefore particularly useful in gene therapy, especially when the gene encodes a protein, or the nucleotide molecules are antisense, triplex forming, ribozymes or guide sequences for RNAase P (claimed) which are used to mutate or stop transcription of a particular gene. Such genes/nucleoti de molecules may be expressed in vivo in patients or in cell culture (claimed). For example, endothelial response elements may be used for any gene therapy where systemic distribution is required, whilst large vessel endothelial cell response elements are useful for expression of thrombomodulin in large vessel endothelium to decrease clot propensity at atheromas or in autoimmune diseases; the environmental stimuli response element(s) are useful e.g. to deliver agents whose expression should be increased during increased thrombin/platelet activation or regional trauma. The regulatory elements are also useful as hybridisation probes, in increasing expression of recombinant proteins by

exposure of the encoding construct
to thrombin and in drug screening and design (not claimed).

16. Document ID: AU 707349 B, WO 9605303 A1, AU 9532723 A, EP 777731 A1, US 5695993 A, US 5852171 A
L1: Entry 16 of 16
File: DWPI
Jul 8, 1999

DERWENT-ACC-NO: 1996-139699
DERWENT-WEEK: 199938

TITLE: Isolated endothelial cell protein C/activated protein C receptor - used to inhibit inflammatory responses,
screen for cpds. which alter receptor binding and, by blocking receptor binding, enhance inflammatory response

PRIORITY-DATA:
1994US-0289699
August 12, 1994
1997US-0878283
June 18, 1997

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
AU 707349 B	July 8, 1999	N/A	000	C12N015/12
WO 9605303 A1	February 22, 1996	E	058	C12N015/12
AU 9532723 A	March 7, 1996	N/A	000	C12N015/12
EP 777731 A1	June 11, 1997	E	000	C12N015/12
US 5695993 A	December 9, 1997	N/A	028	C12N005/16
US 5852171 A	December 22, 1998	N/A	000	C07K014/705

APPLICATION-DATA:

PUB-NO	APPL-DATE	APPL-NO	APPL-DESCRIPTOR
AU 707349B	August 9, 1995	1995AU-0032723	N/A
AU 707349B	N/A	AU 9532723	Previous Publ.
AU 707349B	N/A	WO 9605303	Based on
WO 9605303A1	August 9, 1995	1995WO-US09636	N/A
AU 9532723A	August 9, 1995	1995AU-0032723	N/A
AU 9532723A	N/A	WO 9605303	Based on
EP 777731A1	August 9, 1995	1995EP-0929335	N/A
EP 777731A1	August 9, 1995	1995WO-US09636	N/A
EP 777731A1	N/A	WO 9605303	Based on
US 5695993A	August 12, 1994	1994US-0289699	N/A
US 5852171A	August 12, 1994	1994US-0289699	Div ex
US 5852171A	June 18, 1997	1997US-0878283	N/A
US 5852171A	N/A	US 5695993	Div ex

INT-CL (IPC): A61K 38/17; A61K 39/395; C07H 21/04; C07K 14/705; C07K 16/28; C12N 5/16; C12N 15/11; C12N 15/12; G01N 33/68

IN: ESMON, C T, FUKUDOME, K

AB: Isolated endothelial cell protein C/activated protein C receptor (EPCR) is new. Also claimed are:
(1) a nucleotide sequence encoding EPCR; and (2) an antibody or fragment specifically immunoreactive with a
unique epitope of EPCR., USE - EPCR and substances which up-regulate its expression are useful to inhibit
inflammatory responses (claimed). This inhibition is useful in the treatment of, e.g. Gram-negative sepsis,
stroke, thrombosis, septic shock, ARDS and pulmonary emboli. EPCR is also useful to screen for cpds. which
alter its binding to (activated) protein C (claimed). Localising EPCR to surfaces in contact with blood will
render the surfaces anticoagulant as EPCR binds and concentrates the anticoagulant activated protein C at the
surface. Its function can also be enhanced by overexpressing EPCR in endothelium that could be used to coat
vascular grafts in patients with vascular disease, or in stents in cardiac patients. Using blocking cpds. to

prevent (activated) protein C binding to EPCR it is possible to enhance an inflammatory response and so treat solid tumours., Isolated endothelial cell protein C/activated protein C receptor (EPCR) is new. Also claimed are: (1) a nucleotide sequence encoding EPCR; and (2) an antibody or fragment specifically immunoreactive with a unique epitope of EPCR., USE - EPCR and substances which up-regulate its expression are useful to inhibit inflammatory responses (claimed). This inhibition is useful in the treatment of, e.g. Gram-negative sepsis, stroke, thrombosis, septic shock, ARDS and pulmonary emboli. EPCR is also useful to screen for cpds. which alter its binding to (activated) protein C (claimed). Localising EPCR to surfaces in contact with blood will render the surfaces anticoagulant as EPCR binds and concentrates the anticoagulant activated protein C at the surface. Its function can also be enhanced by overexpressing EPCR in endothelium that could be used to coat vascular grafts in patients with vascular disease, or in stents in cardiac patients. Using blocking cpds. to prevent (activated) protein C binding to EPCR it is possible to enhance an inflammatory response and so treat solid tumours., Isolated endothelial cell protein C/activated protein C receptor (EPCR) is new. Also claimed are: (1) a nucleotide sequence encoding EPCR; and (2) an antibody or fragment specifically immunoreactive with a unique epitope of EPCR., USE - EPCR and substances which up-regulate its expression are useful to inhibit inflammatory responses (claimed). This inhibition is useful in the treatment of, e.g. Gram-negative sepsis, stroke, thrombosis, septic shock, ARDS and pulmonary emboli. EPCR is also useful to screen for cpds. which alter its binding to (activated) protein C (claimed). Localising EPCR to surfaces in contact with blood will render the surfaces anticoagulant as EPCR binds and concentrates the anticoagulant activated protein C at the surface. Its function can also be enhanced by overexpressing EPCR in endothelium that could be used to coat vascular grafts in patients with vascular disease, or in stents in cardiac patients. Using blocking cpds. to prevent (activated) protein C binding to EPCR it is possible to enhance an inflammatory response and so treat solid tumours.

Terms	Documents
epcr! or (endothelial! protein! C! receptor!)	

1. Document ID: US 5847085 A

L4: Entry 1 of 21 File: USPT Dec 8, 1998

US-PAT-NO: 5847085
DOCUMENT-IDENTIFIER: US 5847085 A
TITLE: Modified protein C and methods of use thereof

IN: Esmon; Charles T., Smirnov; Mikhail D.

AB: Modified Protein C molecules have been made which substitute the gamma carboxylglutamic acid (Gla) region of another Vitamin K dependent protein, most preferably prothrombin, for the native region of the Protein C. A modified protein C molecules has been made which substitutes the gamma carboxyglutamic acid (Gla) region with the corresponding region of prothrombin. The modified or chimeric protein C has advantages over the wild-type protein C since it is less sensitive to inhibition by some natural antibody inhibitors of protein C (which would otherwise decrease the ability of the protein C to act as an anticoagulant) and which do not need the same cofactors or same amounts of cofactors, and can therefore be effective in patients with lowered levels of the cofactors such as protein S or the lipids present in elevated levels in platelets such as phosphatidyl ethanolamine (PE). The anticoagulant activity of the chimera was tested in normal and factor V Leiden plasma. The chimera was approximately ten times more effective in inhibiting factor V Leiden plasma clotting.

2. Document ID: US 5837843 A

L4: Entry 2 of 21 File: USPT Nov 17, 1998

US-PAT-NO: 5837843
DOCUMENT-IDENTIFIER: US 5837843 A
TITLE: Modified protein C

IN: Smirnov; Mikhail D., Esmon; Charles T.

AB: Modified Protein C molecules have been made which substitute the gamma carboxylglutamic acid (Gla) region of another Vitamin K dependent protein, most preferably prothrombin, for the native region of the Protein C. The modified or chimeric protein C has advantages over the wild-type protein C since it is less sensitive to inhibition by natural inhibitors of protein C (which would otherwise decrease the ability of the protein C to act as an anticoagulant) and which does not need the same cofactors or same amounts of cofactors, and can therefore be effective in patients with lowered levels of the cofactors such as protein S or the lipids present in activated platelets such as phosphatidyl ethanolamine (PE).

3. Document ID: US 5831025 A

L4: Entry 3 of 21 File: USPT Nov 3, 1998

US-PAT-NO: 5831025
DOCUMENT-IDENTIFIER: US 5831025 A
TITLE: Human activated protein C and process for preparing same

IN: Ogata; Yoichi, Nouchi; Toshinobu, Nakahira; Shinji

AB: A human Activated Protein C preparation with a high specific activity of 3500 U/mg or more and substantially free from thrombin or other proteases which can convert Protein C into Activated Protein C is provided. A process for preparing this human Activated Protein C, which involves, contacting a solution of human Activated Protein C, after activation of Protein C with thrombin or other activating protease, with a cation exchanger to allow for adsorption of both thrombin or another activating protease and Activated Protein C to the cation exchanger followed by elution of the human Activated Protein C alone.

4. Document ID: US 5830467 A

L4: Entry 4 of 21 File: USPT Nov 3, 1998

US-PAT-NO: 5830467
DOCUMENT-IDENTIFIER: US 5830467 A
TITLE: Pharmaceutical preparation containing protein C and a thrombolytically active substance

IN: Eibl; Johann, Philapitsch; Anton, Schwarz; Hans Peter

AB: A pharmaceutical preparation contains protein C and a thrombolytically active substance that does not activate protein C. This preparation prevents reocclusion usually occurring in the course of thrombolysis therapy.

5. Document ID: US 5804392 A

L4: Entry 5 of 21 File: USPT Sep 8, 1998

US-PAT-NO: 5804392
DOCUMENT-IDENTIFIER: US 5804392 A
TITLE: Diagnostic assays using soluble endothelial cell protein C/activated protein C receptor

IN: Esmon; Charles T., Stearns-Kurosawa; Deborah J., Kurosawa; Shinichiro

AB: Plasma EPCR has been isolated, characterized and shown to block cellular protein C activation and
APC anticoagulant activity. Plasma EPCR appears to be about 43,000 daltons and circulates at approximately
100 ng/ml (98.4.+-.27.8 ng/ml, n=22). Plasma EPCR bound activated protein C with an affinity similar to that
of recombinant soluble EPCR (Kd.sub.app approximately 30 nM), and inhibits both protein C activation on an
endothelial cell line and APC anticoagulant activity in a one-stage factor Xa clotting assay. Soluble plasma
EPCR appears to attenuate the membrane-bound EPCR augmentation of protein C activation and the anticoagulant
function of activated protein C. Soluble EPCR has also been detected in urine. Levels of soluble EPCR can
rise in inflammatory disease associated with vascular injury and appear to be correlated with inflammation
and disease states associated with abnormal coagulation. Since EPCR expression is restricted to larger
vessels and is usually negative in cappillaries, these observations provide a mechanism for analyzing
injury/stimulation of large vessel endothelial cells.

6. Document ID: US 5695993 A

L4: Entry 6 of 21 File: USPT Dec 9, 1997

US-PAT-NO: 5695993
DOCUMENT-IDENTIFIER: US 5695993 A
TITLE: Cloning and regulation of an endothelial cell protein C/activated protein C receptor

IN: Fukudome; Kenji, Esmon; Charles T.

AB: Human protein C and activated protein C were shown to bind to endothelium specifically,
selectively and saturably (Kd=30 nM, 7000 sites per cell) in a Ca.sup.2+ dependent fashion. Expression
cloning revealed a 1.3 kb CDNA that coded for a novel type I transmembrane glycoprotein capable of binding
protein C. This protein appears to be a member of the CD1/MHC superfamily. Like thrombomodulin, the receptor
involved in protein C activation, the endothelial cell protein C receptor (EPCR) function and message are
both down regulated by exposure of endothelium to TNF. Identification of EPCR as a member of the CD1/MHC
superfamily provides insights into the role of protein C in regulating the inflammatory response, and
determination of methods for pharmaceutical use in manipulating the inflammatory response.

7. Document ID: US 5614493 A

L4: Entry 7 of 21 File: USPT Mar 25, 1997

US-PAT-NO: 5614493
DOCUMENT-IDENTIFIER: US 5614493 A
TITLE: Use of human protein C for prevention and treatment of depositions of thrombocytes

IN: Eibl; Johann, Schwarz; Hans-Peter, Lozano-Molero; Miguel

AB: The use of human Protein C for the prevention and treatment of deposition or aggregation of
thrombocytes, microparticles of thrombocytes, and leucocytes is described. In addition, an improved method
for the extra-corporeal treatment of body fluids is disclosed.

8. Document ID: US 5593897 A

L4: Entry 8 of 21 File: USPT Jan 14, 1997

US-PAT-NO: 5593897
DOCUMENT-IDENTIFIER: US 5593897 A
TITLE: Binding of immune complexes by modified forms of C-reactive protein

IN: Potempa; Lawrence A., Anderson; Byron E.

AB: A method of binding aggregated immunoglobulin or immune complexes comprising contacting them with
modified forms of C-reactive protein. The method may be employed for diagnostic and therapeutic purposes and
to deplete fluids of aggregated immunoglobulin or immune complexes. Further, a method of reducing the levels
of immune complexes in a mammal comprising administering modified-CRP to the mammal, and a method of binding
immunoglobulins comprising contacting them with modified C-reactive protein. Also, a method of binding
aggregated immunoglobulin or immune complexes comprising contacting them with antibody to neo-CRP, and a
method of modifying C-reactive protein. Finally, a test kit for detecting or quantitating immune complexes
and a device for removing aggregated immunoglobulin or immune complexes from fluids are disclosed.

9. Document ID: US 5545721 A

L4: Entry 9 of 21 File: USPT Aug 13,

1996

US-PAT-NO: 5545721
DOCUMENT-IDENTIFIER: US 5545721 A
TITLE: Conjugates for the prevention and treatment of sepsis

IN: Carroll; Sean B., Firca; Joseph R., Pugh; Charles, Padhye; Nisha V.

AB: Compositions and methods are described for preventing and treating sepsis in humans and other animals. Surgical patients, low birth weight infants, burn and trauma victims, as well as other individuals at risk can be treated prophylactically. Methods for treating acute infections with advantages over current therapeutic approaches are provided. Conjugates and methods of making conjugates for the prevention and treatment of sepsis are described.

10. Document ID: US 5804392 A

L4: Entry 10 of 21 File: EPAB Sep 8, 1998

PUB-NO: US005804392A
DOCUMENT-IDENTIFIER: US 5804392 A
TITLE: Diagnostic assays using soluble endothelial cell protein C/activated protein C receptor

IN: ESMON, CHARLES T, STEARNS-KUROSAWA, DEBORAH J, KUROSAWA, SHINICHIRO

AB: Plasma EPCR has been isolated, characterized and shown to block cellular protein C activation and APC anticoagulant activity. Plasma EPCR appears to be about 43,000 daltons and circulates at approximately 100 ng/ml (98.4+/-27.8 ng/ml, n=22). Plasma EPCR bound activated protein C with an affinity similar to that of recombinant soluble EPCR (Kdapp approximately 30 nM), and inhibits both protein C activation on an endothelial cell line and APC anticoagulant activity in a one-stage factor Xa clotting assay. Soluble plasma EPCR appears to attenuate the membrane-bound EPCR augmentation of protein C activation and the anticoagulant function of activated protein C. Soluble EPCR has also been detected in urine. Levels of soluble EPCR can rise in inflammatory disease associated with vascular injury and appear to be correlated with inflammation and disease states associated with abnormal coagulation. Since EPCR expression is restricted to larger vessels and is usually negative in cappillaries, these observations provide a mechanism for analyzing injury/stimulation of large vessel endothelial cells.

11. Document ID: US 5695993 A

L4: Entry 11 of 21 File: EPAB Dec 9, 1997

PUB-NO: US005695993A
DOCUMENT-IDENTIFIER: US 5695993 A
TITLE: Cloning and regulation of an endothelial cell protein C/activated protein C receptor

IN: FUKUDOME, KENJI, ESMON, CHARLES T

AB: Human protein C and activated protein C were shown to bind to endothelium specifically, selectively and saturably (Kd=30 nM, 7000 sites per cell) in a Ca2+ dependent fashion. Expression cloning revealed a 1.3 kb CDNA that coded for a novel type I transmembrane glycoprotein capable of binding protein C. This protein appears to be a member of the CD1/MHC superfamily. Like thrombomodulin, the receptor involved in protein C activation, the endothelial cell protein C receptor (EPCR) function and message are both down regulated by exposure of endothelium to TNF. Identification of EPCR as a member of the CD1/MHC superfamily provides insights into the role of protein C in regulating the inflammatory response, and determination of methods for pharmaceutical use in manipulating the inflammatory response.

12. Document ID: US 5593897 A

L4: Entry 12 of 21 File: EPAB Jan 14, 1997

PUB-NO: US005593897A
DOCUMENT-IDENTIFIER: US 5593897 A
TITLE: Binding of immune complexes by modified forms of C-reactive protein

IN: POTEMPA, LAWRENCE A, ANDERSON, BYRON E

AB: A method of binding aggregated immunoglobulin or immune complexes comprising contacting them with modified forms of C-reactive protein. The method may be employed for diagnostic and therapeutic purposes and to deplete fluids of aggregated immunoglobulin or immune complexes. Further, a method of reducing the levels of immune complexes in a mammal comprising administering modified-CRP to the mammal, and a method of binding immunoglobulins comprising contacting them with modified C-reactive protein. Also, a method of binding aggregated immunoglobulin or immune complexes comprising contacting them with antibody to neo-CRP, and a method of modifying C-reactive protein. Finally, a test kit for detecting or quantitating immune complexes and a device for removing aggregated immunoglobulin or immune complexes from fluids are disclosed.

13. Document ID: US 5545721 A

L4: Entry 13 of 21

File: EPAB

Aug 13, 1996

PUB-NO: US005545721A
DOCUMENT-IDENTIFIER: US 5545721 A
TITLE: Conjugates for the prevention and treatment of sepsis

IN: CARROLL, SEAN B, FIRCA, JOSEPH R, PUGH, CHARLES, PADHYE, NISHA V

AB: Compositions and methods are described for preventing and treating sepsis in humans and other
animals. Surgical patients, low birth weight infants, burn and trauma victims, as well as other individuals
at risk can be treated prophylactically. Methods for treating acute infections with advantages over current
therapeutic approaches are provided. Conjugates and methods of making conjugates for the prevention and
treatment of sepsis are described.

14. Document ID: AU 9882694 A, US 5804392 A, WO 9900673 A1

L4: Entry 14 of 21

File: DWPI

Jan 19, 1999

DERWENT-ACC-NO: 1998-505645
DERWENT-WEEK: 199922
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TITLE: Immuno-based detection of protein C receptor - useful in the diagnosis of inflammatory and coagulation
states and disorders associated with damage to endothelium and large blood vessel disease

IN: ESMON, C T, KUROSAWA, S, STEARNS-KUROSAWA, D J

AB: An assay for soluble endothelial protein C receptor comprises containing a sample from a patient
to be tested and measuring the amount of soluble endothelial protein C receptor., Also claimed is a kit for
detection and measurement of endothelial protein C receptor comprising:, (a) an antibody immunoreactive with
endothelial protein C receptor:, (b) reagents to detect a reaction between the Ab and endothelial protein C
receptor in a patient sample; and, (c) standards to correlate the amount of reaction to normal and abnormal
levels of endothelial protein C receptor., USE - The assay is used for the diagnosis of coagulation and
inflammatory states and disorders, damage to endothelium, and large blood vessel disease, e.g. autoimmune
diseases, transplantation, sepsis, shock, pre-eclampsia, diabetes, vascular disease (especially
cardiopulmonary bypass, unstable angina, restenosis and angioplasty), kidney disease and liver disease
(claimed). Protein C is involved in the regulation of a host response to inflammation. The protein is one of
the last components to be activated in the coagulation system, and is thought to control coagulation and
inflammation. Activation of the receptor through a pathway involving thrombin, activates protein C. The
protein C pathway is apparently only involved in large blood vessels, not capillaries, and so is activated
with for major vascular conditions, and the increased presence of the receptor in the conditions stated makes
it ideal as a diagnostic component.

15. Document ID: EP 946715 A1, WO 9820118 A1, AU 9851733 A, US 5837843 A, US 5847085 A

L4: Entry 15 of 21

File: DWPI

Oct 6, 1999

DERWENT-ACC-NO: 1998-286934
DERWENT-WEEK: 199946
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TITLE: Protein C chimeric proteins for use as anticoagulants - having gamma carboxyglutamic acid region
replaced with Vitamin K dependent clotting factor e.g. prothrombin

IN: ESMON, C T, SMIRNOV, M, SMIRNOV, M D

AB: Protein C chimeric protein (PCCP) having the gamma carboxylglutamic acid (GCA) region replaced
with the GCA region of prothrombin, is new, Also claimed are:, (1) a nucleic acid molecule encoding a PCCP;,
(2) a method of treating a patient which comprises administering a composition comprising a PCCP where the
GCA region has been replaced with the GCA region of another Vitamin K dependent clotting factor., USE - The
modified PCCPs can be used as anticoagulants, to treat disorders where protein S is low, some forms of lupus,
following stroke or myocardial infarction, after venous thrombosis and in disseminated intravascular
coagulation, septic shock, adult respiratory distress syndrome, pulmonary emboli, warfarin anticoagulation,
in thromboembolic disease or factor V Leiden. Since the chimaera's optimal activity does not depend on normal
levels of protein S in the patient, it is expected to be an active anticoagulant in conditions where the
patient's own activated protein C or therapeutically administered protein C or activated protein C would be
compromised., Protein C chimeric protein (PCCP) having the gamma carboxylglutamic acid (GCA) region replaced
with the GCA region of prothrombin, is new, Also claimed are:, (1) a nucleic acid molecule encoding a PCCP;,
(2) a method of treating a patient which comprises administering a composition comprising a PCCP where the
GCA region has been replaced with the GCA region of another Vitamin K dependent clotting factor., USE - The
modified PCCPs can be used as anticoagulants, to treat disorders where protein S is low, some forms of lupus,
following stroke or myocardial infarction, after venous thrombosis and in disseminated intravascular
coagulation, septic shock, adult respiratory distress syndrome, pulmonary emboli, warfarin anticoagulation,
in thromboembolic disease or factor V Leiden. Since the chimaera's optimal activity does not depend on normal
levels of protein S in the patient, it is expected to be an active anticoagulant in conditions where the
patient's own activated protein C or therapeutically administered protein C or activated protein C would be
compromised., Protein C chimeric protein (PCCP) having the gamma carboxylglutamic acid (GCA) region replaced
with the GCA region of prothrombin, is new, Also claimed are:, (1) a nucleic acid molecule encoding a PCCP;,
(2) a method of treating a patient which comprises administering a composition comprising a PCCP where the
GCA region has been replaced with the GCA region of another Vitamin

K dependent clotting factor., USE - The
modified PCCPs can be used as anticoagulants, to treat disorders where protein S is low, some forms of lupus,
following stroke or myocardial infarction, after venous thrombosis and in disseminated intravascular
coagulation, septic shock, adult respiratory distress syndrome, pulmonary emboli, warfarin anticoagulation,
in thromboembolic disease or factor V Leiden. Since the chimaera's optimal activity does not depend on normal
levels of protein S in the patient, it is expected to be an active anticoagulant in conditions where the
patient's own activated protein C or therapeutically administered protein C or activated protein C would be
compromised.

16. Document ID: US 5593897 A
L4: Entry 16 of 21
File: DWPI
Jan 14, 1997

DERWENT-ACC-NO: 1997-099480
DERWENT-WEEK: 199709
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TITLE: Binding aggregated immunoglobulin and immune complexes - using modified C-reactive protein expressing
neo-CRP antigenicity, for therapeutic removal from body fluid or for analysis

IN: ANDERSON, B E, POTEMPA, L A

AB: Aggregated immunoglobulin (Ig) or immune complexes (IC) are bound by treatment with modified
C-reactive protein (I) that expresses neo-CRP antigenicity. Also new are devices and packages for removing
aggregated Ig or IC from fluids comprising (I) bound to a solid surface, encased in a container., USE - The
method is used: (i) to remove aggregated Ig and IC from mammalian body fluids (esp. for therapeutic use with
the treated fluid returned to the body after treatment but also for treating fluids intended for separate
therapeutic or diagnostic use); or (ii) for detection and quantitation of IC for diagnosis of disease (both
claimed). Other uses include: (a) reducing levels of IC by admin. of (I) to a mammal; and (b) binding
(aggregated) Ig or IC with antibodies to neo-CRP. Diseases which may benefit by removal of IC include cancer,
autoimmune diseases (e.g. myasthenia gravis or multiple sclerosis), arthritis and infections., ADVANTAGE -
(I) is selective for the aggregated form of Ig with very low reactivity for the monomer.

17. Document ID: AU 707349 B, WO 9605303 A1, AU 9532723 A, EP 777731 A1, US 5695993 A, US 5852171 A
L4: Entry 17 of 21
File: DWPI
Jul 8, 1999

DERWENT-ACC-NO: 1996-139699
DERWENT-WEEK: 199938
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TITLE: Isolated endothelial cell protein C/activated protein C receptor - used to inhibit inflammatory
responses, screen for cpds. which alter receptor binding and, by blocking receptor binding, enhance
inflammatory response

IN: ESMON, C T, FUKUDOME, K

AB: Isolated endothelial cell protein C/activated protein C receptor (EPCR) is new. Also claimed are:
(1) a nucleotide sequence encoding EPCR; and (2) an antibody or fragment specifically immunoreactive with a
unique epitope of EPCR., USE - EPCR and substances which up-regulate its expression are useful to inhibit
inflammatory responses (claimed). This inhibition is useful in the treatment of, e.g. Gram-negative sepsis,
stroke, thrombosis, septic shock, ARDS and pulmonary emboli. EPCR is also useful to screen for cpds. which
alter its binding to (activated) protein C (claimed). Localising EPCR to surfaces in contact with blood will
render the surfaces anticoagulant as EPCR binds and concentrates the anticoagulant activated protein C at the
surface. Its function can also be enhanced by overexpressing EPCR in endothelium that could be used to coat
vascular grafts in patients with vascular disease, or in stents in cardiac patients. Using blocking cpds. to
prevent (activated) protein C binding to EPCR it is possible to enhance an inflammatory response and so treat
solid tumours., Isolated endothelial cell protein C/activated protein C receptor (EPCR) is new. Also claimed
are: (1) a nucleotide sequence encoding EPCR; and (2) an antibody or fragment specifically immunoreactive
with a unique epitope of EPCR., USE - EPCR and substances which up-regulate its expression are useful to
inhibit inflammatory responses (claimed). This inhibition is useful in the treatment of, e.g. Gram-negative
sepsis, stroke, thrombosis, septic shock, ARDS and pulmonary emboli. EPCR is also useful to screen for cpds.
which alter its binding to (activated) protein C (claimed). Localising EPCR to surfaces in contact with blood
will render the surfaces anticoagulant as EPCR binds and concentrates the anticoagulant activated protein C
at the surface. Its function can also be enhanced by overexpressing EPCR in endothelium that could be used to
coat vascular grafts in patients with vascular disease, or in stents in cardiac patients. Using blocking
cpds. to prevent (activated) protein C binding to EPCR it is possible to enhance an inflammatory response and
so treat solid tumours., Isolated endothelial cell protein C/activated protein C receptor (EPCR) is new. Also
claimed are: (1) a nucleotide sequence encoding EPCR; and (2) an antibody or fragment specifically
immunoreactive with a unique epitope of EPCR., USE - EPCR and substances which up-regulate its expression are
useful to inhibit inflammatory responses (claimed). This inhibition is useful in the treatment of, e.g.
Gram-negative sepsis, stroke, thrombosis, septic shock, ARDS and pulmonary emboli. EPCR is also useful to
screen for cpds. which alter its binding to (activated) protein C (claimed). Localising EPCR to surfaces in
contact with blood will render the surfaces anticoagulant as EPCR binds and concentrates the anticoagulant
activated protein C at the surface. Its function can also be enhanced by overexpressing EPCR in endothelium
that could be used to coat vascular grafts in patients with vascular disease, or in stents in cardiac
patients. Using blocking cpds. to prevent (activated) protein C binding to EPCR it is possible to enhance an
inflammatory response and so treat solid tumours.

18. Document ID: US 5831025 A, WO 9511966 A1, JP 07115972 A, AU 9480032 A, EP 726311 A1, AU 680563 B, EP 726311 A4, CN 1138349 A

L4: Entry 18 of 21

File: DWPI

Nov 3, 1998

DERWENT-ACC-NO: 1995-178860
DERWENT-WEEK: 199851
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TITLE: Human activated protein C having high specific activity - is prepd. by activating protein C with thrombin, adsorbing the thrombin and activated protein C on a cation exchanger and eluting only the activated protein C

IN: NAKAHIRA, S, NOUCHI, T, OGATA, Y

AB: Human activated protein C prepn., substantially free from thrombin or equivalent protease and/or non-activated protein C, has a specific activity >3500 units/mg based on an activity index of the amt. required to double the activated partial thromboplastin time (APTT). Also claimed is a method of purificn. of protein C obtd. by treatment with a thrombin or a protease, adjusting pH of thus activated protein C to 5-6 and salt concn. to 80 mM, adsorbing the thrombin and activated protein C on a cation exchanger and changing the concn. to 0.1-0.35 M., USE - The cpd. has potential medical use due to its ability to aid plasminogen activator prodn. from blood vessel walls., Human activated protein C prepn., substantially free from thrombin or equivalent protease and/or non-activated protein C, has a specific activity >3500 units/mg based on an activity index of the amt. required to double the activated partial thromboplastin time (APTT). Also claimed is a method of purificn. of protein C obtd. by treatment with a thrombin or a protease, adjusting pH of thus activated protein C to 5-6 and salt concn. to 80 mM, adsorbing the thrombin and activated protein C on a cation exchanger and changing the concn. to 0.1-0.35 M., USE - The cpd. has potential medical use due to its ability to aid plasminogen activator prodn. from blood vessel walls.

19. Document ID: EP 629407 A2, AU 680894 B, DE 4320294 A1, AU 9461719 A, NO 9402298 A, HU 67074 T, CZ 9401482 A3, CA 2126135 A, FI 9402941 A, JP 07048275 A, SK 9400748 A3, EP 629407 A3, US 5614493 A

L4: Entry 19 of 21

File: DWPI

Dec 21, 1994

DERWENT-ACC-NO: 1995-024043
DERWENT-WEEK: 199741
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TITLE: Use of Protein C for prevention and treatment of depositions of thrombocytes - esp. applicable to dialysis appts. and artificial kidneys

IN: EIBL, J, LOZANO-MOLERO, M, SCHWARZ, D H, SCHWARZ DOZ, H, SCHWARZ, H, LOZANO-MOLERO, M D, SCHWARZ, H D

AB: The use of human protein C (I) for the prepn. of a compsn. (C) for the prevention and treatment of deposition and/or aggregation of thrombocytes, microparticles of thrombocytes (dust) and leucocytes with pro-coagulatory activity on vessel surfaces and/or vessel stenoses, esp. on injured, virus-infected or damaged endothelium or on exposed subendothelium or artificial vessel surfaces or vessel prostheses with or without endothelium, is new. Also claimed are the prevention of deposition or aggregation of thrombocytes in vitro by the addn. of (I); and the prevention of deposition and/or aggregation of thrombocyte s in a circulation appts. for the extra-corporeal treatment of body fluids by adding (I) to the extra-corporeally-treated body fluid., USE - The method can be applied to a dialysis appts. or an artificial kidney. (C) is useful for the prevention of arterial restenosis. (I) can be used with all interventions of angioplasty but also with the use of a catheter, in order to prevent negative interactions with stimulated thrombocytes among themselves, with leucocytes, and with the endothelium., Method for preventing a thromboembolic condition caused by deposition or aggregation of blood components selected from the group consisting of thrombocytes, thrombocyte microparticles and leukocytes occurring on a vessel surface or endothelium of a patient, comprising the step of administering to the patient a pharmaceutical composition comprising native protein C in a zymogen form.

20. Document ID: AU 693433 B, WO 9414437 A1, AU 9462269 A, EP 679083 A1, US 5545721 A, JP 08504824 W

L4: Entry 20 of 21

File: DWPI

Jul 2, 1998

DERWENT-ACC-NO: 1994-234320
DERWENT-WEEK: 199837
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TITLE: Antibiotic-antibody conjugate(s), useful for treating e.g. sepsis, burns, trauma etc. - comprises antibiotic or endotoxin covalently bound to non-specific immunoglobulin having Fc region

IN: CARROLL, S B, FIRCA, J R, PADHYE, N V, PUGH, C S G, PUGH, C

AB: Antibiotic-antibody conjugate (A) is capable of binding to bacteria via the antibiotic. (A) comprises an antibiotic or endotoxin binding cpd., covalently bound to a non-specific immunoglobulin (Ig) having an Fc region, pref. Ig capable of binding to phagocytic cells via the Fc region., USE/ADVANTAGE - (A) May be used for preventing and treating sepsis in humans and other animals such as neo-natal calves and foals. Surgical patients, low birth weight infants, burn and trauma victims and immuno-compromised patients can be treated prophylactically. They may also be used as diagnosis. The "antibodiotic" has many effects of the antibiotic alone, without the toxicity and short half-life typical of these agents. The conjugates also possess the opsonising function of Ig, which may facilitate clearance of both the toxin and organism., A

method of synthesizing a non-specific immunoglobulin-antibiotic conjugate comprising the steps of:, a)
reacting an antibiotic that binds to the surface of microorganisms with a first bifunctional crosslinking
agent, to form a crosslinker derivatized antibiotic;, b) reacting non-specific immunoglobulin with a second
bifunctional crosslinking agent, to form a crosslinker derivatized non-specific immunoglobulin; and, c)
reacting said crosslinker derivatized antibiotic with said crosslinker derivatized non-specific
immunoglobulin to form a covalent bond between said first and second bifunctional crosslinking agents to form
a non-specific immunoglobulin-antibiotic conjugate that binds to the surface of microorganisms via the
antibiotic.

21. Document ID: US 5830467 A, EP 519900 A1, AU 9218304 A, CA 2071625 A, JP 05170665 A, AU 656199 B, AT 9101240 A, AT 402263 B
L4: Entry 21 of 21
File: DWPI
Nov 3, 1998

DERWENT-ACC-NO: 1992-426081
DERWENT-WEEK: 199851

TITLE: Drug compsn. for preventing re-occlusion during thrombolytic therapy - contains antithrombotic agent
(e.g. urokinase), and protein C

IN: EIBL, J, PHILAPITSCH, A, SCHWARZ, H P, SCHWARZ DOZ, H P

AB: Pharmaceutical compsns. contains protein C and a thrombolytic agent (I) which does not activate
proein C., Pref. (I) is urokinase, tissue plasminogen activator, Lys-plasminogen or streptokinase.,
USE/ADVANTAGE - The compsns. are useful for thrombosis therapy. Addn. of a non-activated protein C
counteracts plasmin-induced degradation of the plasma protein C following thrombolysis, thereby inhibiting
vascular reocclusion without causing excessive bleeding due to the presence of activated protein C,
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